CHEM-342 Introduction to Biochemistry
Final Examination - Group (Part II)
Tuesday, 24 May 2011
9:00 – 10:00 PM
H. B. White – Instructor

40 Points

Group Members

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Important - Please read this before you turn the page.

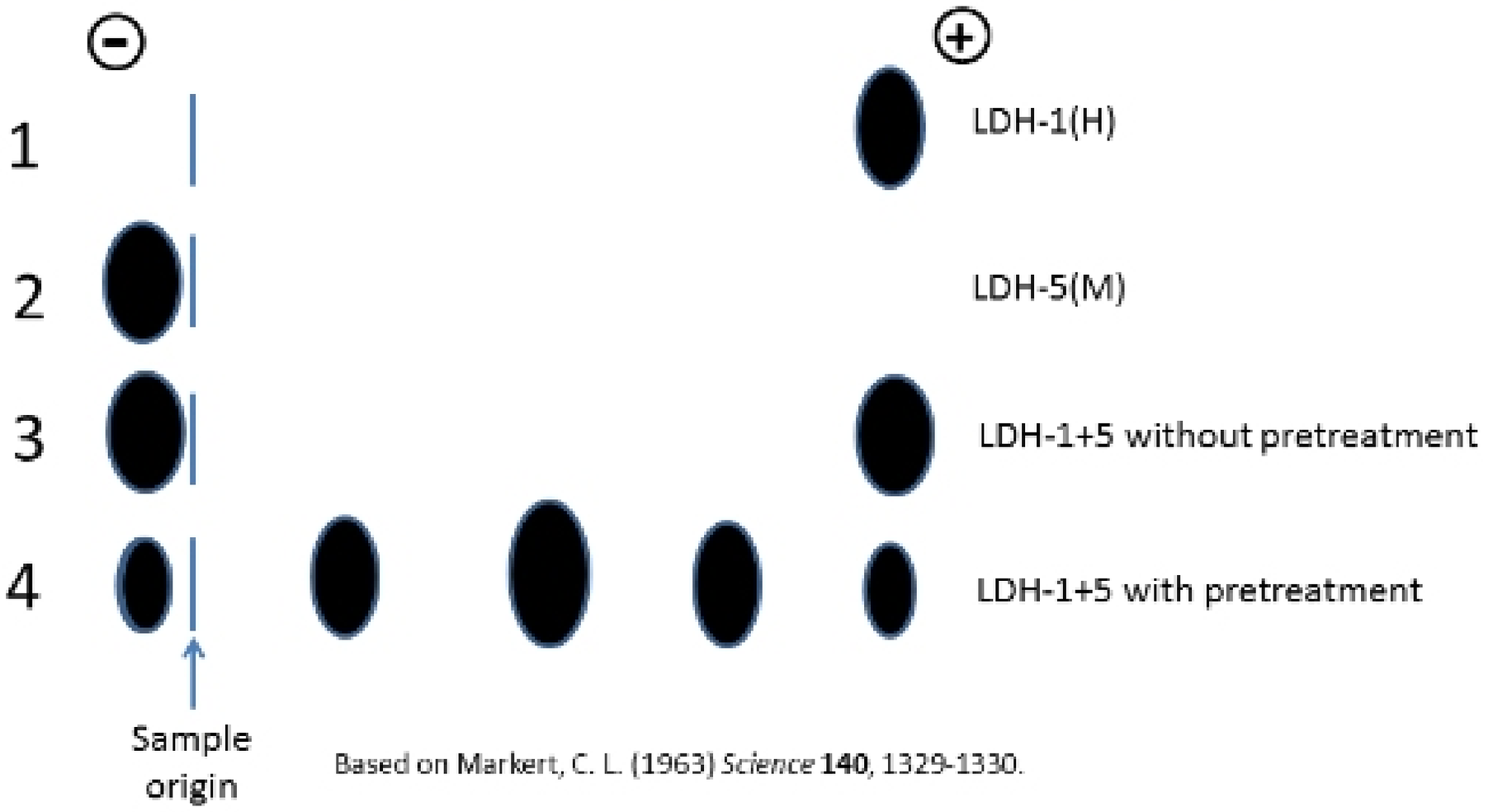
- You must sign your name on this page to receive the group grade.
- You may refer to your notes, course reader, handouts, or graded homework assignments.
- In CHEM-342, hemoglobin is a vehicle for learning how to learn by asking questions and pursuing answers to those questions. Undoubtedly you have learned a lot about hemoglobin in the process but you also should be developing habits of mind that will enable you to solve problems in other courses and throughout your life. This part of the final examination provides an opportunity for you and the other members of your group to display problem-solving skills as a team. It is extremely unlikely that anyone in your group or in the class has encountered the information on the following pages. Your answers should display your collective:
- breadth of knowledge (not limited to hemoglobin or biochemistry)
- ability to analyze, make connections, and ask probing questions
- sense of logic and organization
- skill at generating models (testable hypotheses)

http://dsc.discovery.com/news/2008/09/04/gallery/woolly-mammoth-324x205.jpg

1. (15 points) Woolly mammoths went extinct near the end of the last ice age. However, DNA from mammoths frozen in permafrost has been isolated and the nucleotide sequence of the hemoglobin alpha and beta-like genes has been determined. Less than a year ago, researchers reported that they had cloned and expressed the genes producing functional mammoth hemoglobin. [Campbell, K. L. et al. *Nature Genetics*, **42**, 536-540 (2010)]

   Research costs money and thus experiments that address interesting questions have higher priority than those that don't. Based on your knowledge of hemoglobin (and mammoths), make a list of three things you would recommend researchers should study. Please describe in several sentences why you think each of your suggestions would be interesting to do.

2. Functional hemoglobin has an $\alpha_2\beta_2$ structure with the α and β subunits being similar in structure, but encoded by separate genes and having different amino acid sequences. The phenomenon of having a discrete complex of multiple, but similar or identical, subunits that assemble to form an active protein is quite common in nature. For example, the glycolytic enzyme, lactate dehydrogenase, is a multimeric protein whose subunit structure was deduced in the 1960's using electrophoresis and other methods. In mammals there is one gene encoding subunits for LDH-1(H) that is most active in heart and another gene most active in skeletal muscle encoding subunits for LDH-5(M). In tissues like liver, both genes are active to different extents generating hybrid LDH "isozymes". The various LDH isozymes are stable complexes and separate on electrophoresis as shown below. If purified LDH-1 (lane 1) is mixed with purified LDH 5 (lane 2) and frozen overnight in 1M NaCl, the pattern observed in lane 3 becomes the pattern observed in lane 4 with three new isozymes corresponding to those seen *in vivo*.



Based on Markert, C. L. (1963) *Science* **140**, 1329-1330.

A. (8 points) From the patterns observed, generate a model of how monomers assemble into the active multimers.